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Comparison of Prognosis in Patients with Liver Cirrhosis and its Correlation with the Model for the End-Stage Liver Disease and Child-Pugh Score in Two Groups of Esophageal and Gastric Variceal Bleeding

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Abstract

Background: Variceal bleeding is one of the most serious complications of cirrhosis. Up to now different methods are created for predicting the complications and mortality of cirrhosis. Child- Pugh score and MELD score are two methods for this use. In this study we investigated and compared survival prognosis of cirrhotic patients by the Child-Pugh or MELD score in two groups of esophageal and gastric variceal bleeding. **Materials and Methods:** In this cross-sectional trial, patients with upper GI bleeding were followed up for a 6 months period. The source of hemorrhage was determined by endoscopy, then patients distributed in two groups of esophageal and gastric variceal hemorrhage. Finally we investigated and compared the relationship between the variables and mortality rates in these two groups by means of the Child-Pugh and the MELD scores. The Student's t-test and Receiver Operating Characteristic were used for statistical analysis. **Results:** 34 patients (12 with gastric varices, 22 with esophageal varices) were investigated. No significant difference between these two groups was observed. In this study mean MELD score was 16.67±8.75 and mean Child-Pugh score was 9.37±2.54. Eight patients (5 with gastric varices and 3 with esophageal varices) expired before 6 weeks and 2 patients (one four each group) expired after 6 weeks. The best cut-off points are 15.5 and 10.5 for MELD and Child-Pugh scores respectively (sensitivity and specificity are 0.75 and 0.98, respectively for both scores). **Conclusion:** Sensitivity and specificity of both scores were the same in prediction of mortality. However, the chance ratio defined that Child-Pugh score was a better predictor of mortality than MELD score, since the chance of death will increase 2.51 and 1.62 fold per each unit increase in the Child-Pugh and the MELD scores, respectively. However, no significant difference found between Child-Pugh and MELD score between two groups of patients. **[GMJ. 2013;2(3):106-113]**

Keywords: Liver Diseases; Esophageal Varices; Gastric Varices; Mortality

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Introduction

Variceal hemorrhage is one of the most serious complications of cirrhosis that leads to 13-30% mortality [1-3]. Variceal hemorrhage's predisposing factors are size, shape, pressure, and place of varices and also other clinical manifestations of underline diseases [4]. The varices commonly expand in distal portion of esophagus, stomach and rectum; however other parts of the gastrointestinal tract can be affected [5]. Varices in middle portion of esophagus are formed deeply in the sub-mucosal layer and have mucosal support but in distal portion varices are more superficial and have less mucosal support, so they have more susceptibility for bleeding. Gastric varices' hemorrhages are also common. These varices can be the continuation of esophageal varices in greater or lesser curvature (GOV-1=Type 1 gastroesophageal varices) or it can be isolated in fundus (IGV1= type 1 isolated gastric varices) with prevalence of 10% and 90% respectively [6]. The more serious chronic hepatic disease takes place with the more complications and the more mortality because of hypovolumic shock, infections, and hepatic failure [7, 8]. Up to now different methods are created to predict the complications and mortality rate of cirrhosis. One of the most common and usable occupied methods is Child-Pugh score method [9]. However, this method can lead to some restrictions because of having two subjective criteria such as encephalopathy and acites. Recently, MELD (Model for the End-Stage Liver Disease) score is brought up as another prediction method of complications and mortality rates. This score is calculated by 3 biochemical parameters. Nevertheless the complexibility of this formula is regarded as a restriction [10-13]. Many studies have shown that a higher Child-Pugh or MELD score is associated with a greater mortality rate [14]; also some of others have shown the predicting value of these methods [15-17]. The overall results of these studies showed that thirty-day mortality after acute variceal bleeding is 15-20%. However, mortality rates of patients within six weeks after the bleeding was increased but the rate of survival after six weeks bleeding in cirrhotic patients was the same as those without bleeding [2].

In this study we investigated and compared Child-Pugh score versus MELD score in two groups of esophageal variceal bleeding and gastric variceal bleeding patients with cirrhosis and also we compared mortality rates between these two groups. The innovation of our study is this comparison and also the determination of cut-off point value of these methods in Iranian cirrhotic patients.

Materials and Methods

In our cross-sectional study, all the patients with upper GI (gastrointestinal) bleeding who were referred to Imam Reza Hospital Emergency ward from September 2011 to December 2012 were enrolled according to laboratory evalutions and then patients were followed up for a 6 months period. Our study's inclusion criteria were: diagnosis of cirrhosis with any etiologies, occurrence of hematemesis or melena within 24 hours with vaiceal source before admission, and the first time incidence of upper GI bleeding. Also patients were excluded if they had GI bleeding with non-cirrhotic source, congestive gastropathy, ectopic varices, and hepatocellular carcinoma. All the participants were allowed to exit the study at any time during the investigations. The variables that were investigated in this study were: age, sex, bilirubin, albumin, INR, creatinine, acites, hepatic encephalopathy, mortality rates in the first 6 weeks after the initial bleeding up to 6 months.

Diagnostic methods for cirrhosis were histological, clinical and biochemical profile results and also sonographic and endoscopic investigations. We determined the source of hemorrhage in cirrhotic patients by endoscopy, so we distributed the patients in two groups of esophageal variceal hemorrhage and gastric variceal hemorrhage.

For calculation of the Child-Pugh score we used the main formula (Table-1) [18].Child-Pugh score consists of 5 parameters: bilirubin, albumin, INR, ascites, and hepatic encephalopathy. MELD score has been calculated using the following formula by the Mayo-Clinic group [19]: MELD SCORE: 10 {0.957 Ln

Table 1. Child Pugh score parameters

Parameters	1 point	2 point	3 point
Serum bilirubin total (mg/dL)	<34 (<2)	34-50 (2-3)	>50(>3)
Serum albumin (mg/dL)	>35	28-35	<28
INR	<1.7	1.71-2.20	>2.20
Ascites	Non	Suppressed with medication	Refractory
Hepatic encephalopathy	Non	Suppressed with medication	Refractory

[creatinine (mg/dL)] + 0.378 Ln [bilirubin (mg/dL)] + 1.12 Ln INR + 0.643}

Finally we investigated and compared the relationship between the variables and mortality rates in these two groups.

Mashhad University of Medical Sciences Research Ethics Council approved the project and the consents were freely and knowingly filled by the subjects. Satistical analysis performed by SPSS 17.0 and data explained as mean ± standard deviation and P <0.05 considered as significant. We used Sample T-Test and Mann-Withney test to analyse quantitative variables and also we used $\chi 2$ test and Fischer Test to analyse qualitative variables. In order to study the simultaneous effect of the variables in predicting the patient prognosis, we occupied the multiple logistic regressions. Also we used Receiver Operating Characteristic (ROC) curve to determine the appropriate cut-off points with suitable specificity and sensitivity for MELD and Child-Pugh scores.

Results

During this study 131 patients were enrolled in this study according to inclusion criteria but 97 patients were excluded according to exclusion criteria or exited in the follow up period and at last 34 patients were taken into account. Among those who excluded, 17 patients had congestive gastropathy, 2 patients had ectopic varices, 3 patients had hepatocellular carcinoma, 20 patients exited willingly, 13 patients were not available for the follow up, 42 patients had other bleeding sources. From 34 remained patients, 12 of them had gastric varices and 22 of them had esophageal varices. No significant differences between these two groups were observed regarding the demographic data (Table-2). In this study mean MELD score was 16.67±8.75 and mean Child-Pugh score was 9.37±2.54. Eight patients (5 with gastric varices and 3 with esophageal varices) expired before 6 weeks and 2 patients (one with gastric varices and one with esophageal varices) expired after 6 weeks. Fischer exact test showed that there was no significant relationship between the mortality and the patient groups (P=0.09). From 24 alive patients 16 were men and 8 were women (P=0.08). Also, there was no significant difference regarding the mean age of the expired patinent and the alive ones (P=0.76; t=0.31). Study of two important liver function markers, AST and ALT, showed that there were significant differences between expired and alive groups (P=0.001; P=0.004). MELD and Child-Pugh score were significantly higher in expired groups than the alive ones (P=0.001 and P<0.001, respectively; Table-3). To investigate the mortality predicting power of Child-Pugh or MELD scores, logistic regression analysis was used. Results showed that both MELD and Child-Pugh scores can predict the mortality of the patients along as if MELD scores increase one score, then the mortality rate will be 1.62 fold higher (P=0.006) and if Child-Pugh scores increase one score, then the mortality rate will be 2.51 fold higher (P=0.004). To get the appropriate cut-off points for MELD and Child-Pugh scores we used ROC. According to ROC results, 26 is an appropriate cut-off point for MELD score for prediction of mortality with a sensitivity and specificity of 0.75 (95% CI=0.58-0.92) and 0.98 (95% CI=0.55-1), respectively, while it is 11.5 for Child-Pugh score with a sensitivity and specificity of 0.75 (95% CI=0.59-0.91) and 0.98 (95% CI=0.71-1), respectively, (Figure-1, 2). The areas under the curve with 95% CI were 0.72-0.98 for MELD score and 0.81-1 for Child-Pugh score.

Table 2. Clinical and biochemical characteristics, MELD and Child-Pugh between two

Parameters	Gastric varic (n=12)	Esophageal varic (n=22)	Power	P-value
Sex(M/F)‡	8/4	15/7	0.03	>0.99
Age(year)(SD)†	60.75 (19.03)	56.59 (14.18)	0.1	0.47
ALT (mg/dL) [IQR]*	87.5 [80.25]	35.5 [55.25]	0.29	0.34
AST(mg/dL) [IQR]*	84 [97]	52 [53.75]	0.16	0.42
Serum albumin (mg/dL) (SD)†	2.76 (0.37)	2.92 (0.36)	0.21	0.23
Serum bilirubin (mg/dL) [IQR]*	1.15 [3.75]	1.45 [2.32]	0.08	0.69
Serum creatinine (mg/dL) [IQR]*	1.1 [0.60]	1.1 [0.63]	0.05	0.74
Prothrombin time (second) [IQR]*	15.1 [5.87]	16.2 [7.5]	0.4	0.16
INR[IQR]*	1.35 [0.88]	1.5 [1.05]	0.22	0.24
Ascites (N/M/P)1‡	0/5/7	5/10/7	0.39	0.14
Hepatic encephalopathy (N/M/P)2‡	5/3/4	15/2/5	0.29	0.31
MELD score[IQR]*	14 [18]	14 [14.5]	0.08	0.6
Child-Pugh score(SD)†	10.33 (2.39)	9.41 (2.61)	0.17	0.32

-Values are presented as mean (standard deviation) or median [Inter quartile range] and compared with Mann-Whitney test (*), T student test (†) or Fisher's exact test (‡)
-1 & 2: N: No M: Moderate S: Severe

Table 3. Clinical and biochemical characteristics, MELD and Child-Pugh scores Pugh between two groups of study (Surviving patients vs. Deceased patients)

Parameters	Surviving Patients (n=24)	Deceased Patients (n=10)	Power	P-value
Sex(M/F)‡	16/8	7/3	0.03	>0.99
Age(year)(SD)†	57.5 (16.15)	59.4 (16.04)	0.06	0.76
ALT((mg/dL)) [IQR]*	21 [30.5]	87.5 [20]	0.79	0.00
AST((mg/dL)) [IQR]*	33 [47]	92.5 [35.5]	0.55	0.00
Serum albumin (mg/dL) (SD)†	2.9 (0.37)	2.8 (0.36)	0.11	0.36
Serum bilirubin (mg/dL) [IQR]*	1.3 [1.15]	4.4 [4.87]	0.64	0.12
Serum creatinine (mg/dL) [IQR]*	0.95 [0.38]	1.4 [0.95]	0.45	0.00
Prothrombin time (second) [IQR]*	15.3 [4.33]	19.9 [11.55]	0.62	0.03
INR[IQR]*	1.4 [0.57]	2.2 [2.15]	0.75	0.02
Ascites(N/M/P)1‡	5/13/6	0/2/8	0.73	0.01
Hepatic encephalopathy (N/M/P) 2‡	20/2/2	0/3/7	0.99	0.00
MELD score[IQR]*	11.5 [9]	27 [13.75]	0.91	0.00
Child-Pugh score(SD)†	8.67 (1.99)	12.3 (1.77)	0.99	0.00

- Values are presented as mean (standard deviation) or median [Inter quartile range] and compared with Mann-Whitney test (*), T student test (†) or Fisher's exact test (‡)
-1 & 2: N: No M: Moderate S: Severe

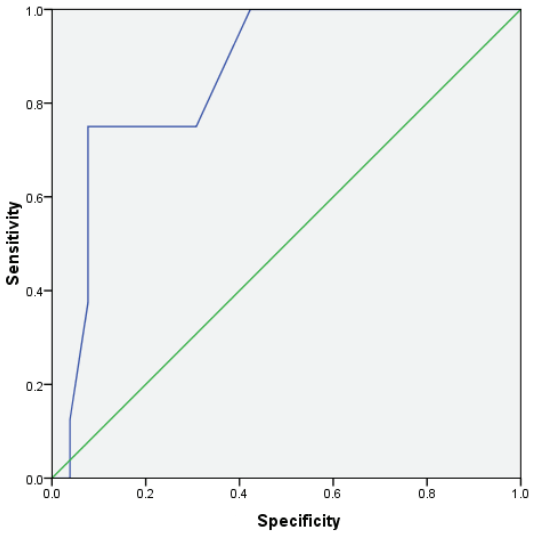

Figure 1. The Receiver Operating Characteristic (ROC) Curve for MELD Score

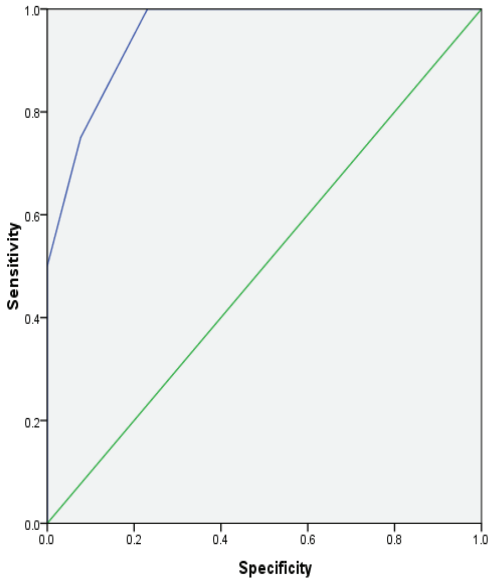

Figure 2. The Receiver Operating Characteristic (ROC) Curve for Child-Pugh Score

Discussion

One of the most challenging topics for physicians in approach to cirrhosis is the evaluation of the patients' prognosis. Appropriate determination of liver transplantation time can reduce the mortality rates in patients waiting for transplantation and also may increase the patient survival [20-23].

Patients with cirrhosis who are suffering from variceal bleeding are in higher risk of mortality, so predicting the prognosis of patients helps us to determine appropriate time of their treatments. Nowadays, Child-Pugh score is one of the most usable methods for evaluating the prognosis of cirrhosis, but it has some shortcomings like its subjective factors (ascites and encephalopathy) which can be impressed by physician judgment. Moreover, this model can not distinguish the difference between 2 mg/dL or 4 mg/dL level of bilirubin as an example, because both of them are classified in the same classes and it is not possible to differentiate patients who are classified in a same group. According to this issue, recent studies investigated the impacts of other parameters like plasma sodium and serum creatinine concentrations on improvement of sensitivity of this method [24-26].On the other hand, MELD score was developed after Child-Pugh score to assess the prognosis of cirrhotic patients. MELD scoring is validated model for staging of chronic liver disease and it uses serum bilirubin, serum creatinine, and INR for prediction of patients' survival and the severity of liver damage. At first, MELD score was created in order to predict mortality in patients with transjugular intrahepatic porto-systemic shunt (TIPS); and after that, it was used in assessing the prognosis of cirrhotic patients with a variety of clinical setting [10-13,27]. Increased MELD scores in cirrhotic patients are associated with hepatic impairment and also mortality rate. Two independent studies which have been conducted in North America, have shown that MELD score is at least as effective as Child-Pugh score in predicting clinical outcomes such as acute variceal bleeding and mortality in patients listed for liver transplantation [28,29]. Our study have confirmed this equivalency and explained the same sensitivity and specificity of 75% and 98% in differentiation of patients' mortality for both models. In another study which was done by Stojanov et al [30] on cirrhotic patients with variceal hemorrhage, sensitivity was 95% for both scores and specificity of MELD and Child-Pugh scores were 53.8 and 82.5, respectively. In other studies [31] there were no significant difference between AUROC (area under the ROC curve) values of these two methods, and in some other stud

ies both Child-Pugh and MELD scores have equivalent predicting power for mortality; however, in one of these studies which have investigated the cirrhotic patients who were waiting for transplantation, MELD score had a more predicting power than Child-Pugh score [32-39]. Although MELD score calculation is more complicated than Child-Pugh score and needs computer analysis, its usage is becoming more preferred [31]; because this method uses objective variables like serum creatinine which is an important parameter in determining the prognosis of patients sufferind fsom chronic liver diseases. Finally, it seems that, due to the favorable results reported for its high sensitivity and specificity, this preference in its usage is logical and might be beneficial for patients and health care providers. The reasons which might explain the better performance of MELD score in the prediction of mortality in cirrhotic patients with variceal hemorrhage in our study are: 1- Patients who died might have some degree of renal failure previously, 2- By increasing severity of bleeding, some degree of hemodynamic instability and acute renal failure due to hypovolumic shock might be occurred, 3- The patients who died were more likely to have liver function impairments. On the other hand, another point in our study is high mortality rate of cirrhotic patients in the first 6 weeks in comparison with other studies. In our investigation mortality rate for esophageal variceal bleeding was 8.8% and for gastric variceal bleeding was 14.7%, whereas in other studies it was 8% for esophageal varices and 14.2-42.7% for gastric varices [29, 31, 40]. These differences can be caused by different prophylactic antibiotics, usage of different interventions, different inclusion criteria, and the study population.

At last we compared Child-Pugh and MELD scores between groups with esophageal variceal and gastric variceal hemorrhages. Results showed that there were no significant differences between these two groups.

The limitations of this study were the use of different PPI treatments plan and administration methods for the participants by different physicians. The other limitation was the relatively small sample size. Due to this limitation, our findings cannot be generalized to the broader community. Therefore, more prospective surveys using the same methods with larger populations are needed to properly identify the better scoring method for prediction of mortality rate.

Conclusion

The results showed that both the Child-Pugh and MELD scoring method are similar considering the sensitivity and specificity in predicting the mortality. However, the chance ratio defined that, Child-Pugh score is a better predictor of mortality than MELD score, since the chance of death will increase 2.51 and 1.62 fold per each unit increase in the Child-Pugh and the MELD scores, respectively. However, no significant difference was found between Child-Pugh and MELD scores between two groups of patients suffering from esophageal and gastric variceal bleeding.

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