**Title: 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

Introduction

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.

Method

In this cohort tiral, patients with the 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 26 and 11.5 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 increasing of the Child-Pugh and the MELD scores, respectively. However, no significant difference found between Child-Pugh or MELD score between two groups of patients.

Introduction

Variceal hemorrhage is one of the most serious complications of cirrhosis that leads to 13-30% mortality ([1-3](#_ENREF_1)). Variceal hemorrhage predisposing factors are size, shape, pressure and place of varices and also other clinical manifestations of background diseases ([4](#_ENREF_4)). The varices commonly expand in distal portion of esophagus, stomach and rectum; however other parts of the gastrointestinal tract can be afflicted ([5](#_ENREF_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; also gastric varices hemorrhage are common too. These varices can be the continuation of esophageal varices in greater or lesser curvature that names (GOV1) or it can be isolated in fundus that names (IGV1) with prevalence of 10% and 90% proportionally ([6](#_ENREF_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](#_ENREF_7), [8](#_ENREF_8)). Up to now different methods are created to predict the complications and mortality rate of cirrhosis. One of the most common and usable used method is Child-Pug score ([9](#_ENREF_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 method prediction of complications and mortality rates. This score is calculated by 3 biochemical parameters. Nevertheless the complexibility of this formula is a restriction for this method ([10-13](#_ENREF_10)).

Many studies have shown that a higher Child-Pugh or MELD score is associated with a greater mortality rate ([14](#_ENREF_14)); also some of others have shown the predicting value of these methods ([15-17](#_ENREF_15)). The overall results of these studies show that thirty-day mortality after acute variceal bleeding is 15-20%. However mortality rates of patients within six weeks after the bleeding has increased but the rate of survival after six weeks bleeding in cirrhotic patients is the same as without bleeding patients ([2](#_ENREF_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.

Methods

In our cohort study we investigate all patients with upper GI bleeding who were referred to Imam Reza Hospital Emergency ward from September 2011 to December 2012 with purposeful sampling and then patients were followed up for a 6 months period. Our study inclusion criteria were diagnosis of cirrhosis with any etiologies, any occurrence of hematemesis or melena within 24 hours before admission with vaiceal source, and the first time incidence of upper gastrointestinal (GI) bleeding. Also patients were excluded if they had GI bleeding with non-cirrhosis source, congestive gastropathy, ectopic varices, hepatocellular carcinoma and dissatisfaction. The variables that were investigates in this study are: age, sex, bilirubin, albumin, INR, creatinine, acites, hepatic encephalopathy, mortality rates in the first 6 weeks after the initial bleeding and also up to 6 months.

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

For calculation of the Child-Pugh score we used the main formula ([18](#_ENREF_18)). (Table 1)

Child-Pugh score consists of 5 parameters: bilirubin, albumin, INR, acites and hepatic encephalopathy. MELD score has been calculated using the following formula by the Mayo Clinic group ([19](#_ENREF_19)): MELD SCORE: 10 {0.957 Ln [creatinine (mg/dL)] + 0.378 Ln [bilirubin (mg/dL)] + 1.12 Ln INR + 0.643}

Finally we investigate 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 consent was freely and knowingly filled by the subjects.

Analysis performed by SPSS 17.0 and data explained as mean ± standard deviation and P <0.05 considered as significant. We use Sample T-Test and Mann-Withney test to analyse quantitative variables and also we use χ2 test and Fischer Test to analyse qualitative variables. In order to study the simultaneous effect of the variables in predicting the patient prognosis, we used 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 score.

Results

During the period of study 131 patients were enrolled to the study according to inclusion criteria but 97 patients were excluded according to exclusion criteria or missing in the follow up periods and at last 34 patients were investigated. Among those who excluded, 17 patients had congestive gastropathy, 2 patinets had ectopic varices, 3 patients had hepatocellular carcinoma, 20 patients had dissatisfaction, 13 patients were not available for the follow up, 42 patients had others bleeding sources. From 34 remained patients, 12 of them had gastric varices and 22 of them had esophageal varices. No significant difference between these two groups was observed with 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 us that there was not significant relationship between mortality and patient groups (P-value=0.098). From 24 patients without mortality 16 of them were men and 8 others were women (p-value=0.084). Also there was no significant difference with age of who were expired and who are alive (P-value=0.76; t=0.313). Study of two important liver function markers such as AST and ALT showed that there were significant differences between expired and alive groups (p-value= 0.001; p-value=0.004). MELD and Child-Pugh score were significantly more in expired groups than alives ( p-value=0.001; p-value>0.001 respectively). (Table 3) To investigate 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 ( p-value=0.006) and if Child-Pugh scores increase one score, then the mortality rate will be 2.51 fold ( p-value=0.004). To get the appropriate cut-off points for MELD and Child-Pugh score we used receiver operating characteristic curve (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 and 0.98 respectively while it is 11.5 for Child-Pugh score whith a sensitivity and specificity of 0.75 and 0.98 respectively (Graphs1, 2).

Discussion

One of the most challenging topics for physicians in approach to cirrhosis is the evaluation of the patient’s 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](#_ENREF_20)).

Patients with cirrhosis who are suffering from variceal bleeding have more risk for mortality, so predicting the prognosis of patients helps up 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 judgments. 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 groups. According to this issue, recent studies investigated the effect of other parameters like sodium serum and serum creatinine on sensitivity improvement of this method ([24-26](#_ENREF_24)).

On the other hand, MELD score was developed after Child-Pugh score to assess the prognosis of cirrhotic patients. MELD scoring is a developed and validated model for chronic liver disease staging and it uses serum bilirubin, serum creatinine, and INR for prediction of patients survival and the severity of liver failure. 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](#_ENREF_10), [27](#_ENREF_27)). Increased MELD scores in cirrhotic patients have a relationship 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](#_ENREF_28), [29](#_ENREF_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](#_ENREF_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](#_ENREF_31)) there were no significant difference between AUROC ([area under the ROC curve](https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=5&ved=0CEoQFjAE&url=http%3A%2F%2Fespace.library.uq.edu.au%2Feserv.php%3Fpid%3DUQ%3A8925%26dsID%3Dpr-t.pdf&ei=olejUcf7F-b44QTu4oD4BQ&usg=AFQjCNH5Fzef_12pZA16-SNShD1-f0mV_A&sig2=tFiccO2z3Dwkg_vsXyZuMQ)) values of these two methods. And in some other studies both Child-Pugh and MELD scores have equivalent predicting power for mortality; however in one of them which had investigated the cirrhotics patients who were waiting for transplantation, MELD score had a more predicting power than Child-Pugh score ([32-39](#_ENREF_32)). Although MELD score calculation is more complicated than Child-Pugh score and needs for computeral analysis but its usage is in progression ([31](#_ENREF_31)); because this method uses objective variables like as serum creatinine which is an important parameter in determining the prognosis of chronic liver diseases patients. Finally it seems that, due to the favorable results reported for its high sensitivity and specificity, this progression in its usage is logical and might be beneficial for patients and medical staffs.

The reasons which might explain for 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 hypovolemic 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 study 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](#_ENREF_29), [31](#_ENREF_31), [40](#_ENREF_40)). These differences can be caused by different usage of prophylactic antibiotics, usage of different interventions and finally different inclusion criteria and study population.

At last we compared Child-Pugh and MELD scores between esophageal variceal and gastric variceal hemorrhage groups and results showed that there was no significant difference between these two groups. The limitations of this study were the use of different PPI treatments plan and administration methods which was used by different physicians. Therefore, another prospective studies using the same treatment plan are needed to properly identify the better score for prediction of mortality in a larger number of patients.

Conclusion

The results showed that both the Child-Pugh and MELD scores are the same with the sensitivity and specificity in predicting 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 increasing of the Child Pugh score and the MELD scores, respectively. However, no significant difference found between Child-Pugh and MELD scores between two groups of esophageal and gastric variceal bleeding patients.

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This manuscript has been read and approved by all of the Authors and there is not potential conflict of interest for them.

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