ORIGINAL ARTICLE UDC 616.36–004+616.329–005.1]:616–036.8–037

The Model for the End-Stage Liver Disease and Child-Pugh score in predicting prognosis in patients with liver cirrhosis and esophageal variceal bleeding

Model terminalnog stadijuma bolesti jetre i Child-Pugh skora u predviđanju prognoze bolesnika sa cirozom jetre i ezofagusnim varikoznim krvarenjima

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Abstract

Background/Aim. Esophageal variceal bleeding is one of the most frequent and gravest complications of liver cirrhosis, directly life-threatening. By monitoring certain clinical and laboratory hepatocellular insufficiency parameters (Child-Pugh score), it is possible to determine prognosis in patients who are bleeding and evaluate further therapy. Recently, the Model for the End-Stage Liver Disease (MELD) has been proposed as a tool to predict mortality risk in cirrhotic patients. The aim of the study was to evaluate survival prognosis of cirrhotic patients by the MELD and Child-Pugh scores and to analyze the MELD score prognostic value in patients with both liver cirrhosis and variceal bleeding. **Methods.** We retrospectively evaluated the survival rate of a group of 100 cirrhotic patients of a median age of 57 years. The Child-Pugh score was calculated and the MELD score was computed according to the original formula for each patient. We also analysed clinical and laboratory hepatocellular insufficiency parameters in order to examine their connection with a 15-month survival. The MELD values were correlated with the Child-Pugh scores. The Student's *t*-test was used for statistical analysis. **Results.** Twenty-two patients died within 15-months follow-up. Age and gender did not affect survival rate. The Child-Pugh and MELD scores, as well as ascites and encephalopathy significantly differed between the patients who survived and those who died ($p < 0.0001$). The International Normalized Ratio (INR) values, serum creatinine and bilirubin were significantly higher, and albumin significantly lower in the patients who died ($p < 0.0001$). The MELD score was significantly higher in the group of patients who died due to esophageal variceal bleeding ($p < 0.0001$). **Conclusion.** In cirrhotic patients the MELD score is an excellent survival predictor at least as well as the Child-Pugh score. Increase in the MELD score is associated with decrease in residual liver function. In the group of patients with liver cirrhosis and esophageal variceal bleeding, the MELD score identifies those with a higher intrahospital mortality risk.

Key words:
liver diseases; liver cirrhosis; esophageal and gastric varices; questionnaires; prognosis.

Apstrakt

Uvod/Cilj. Krvarenje iz varikoziteta najčešća je i najteža komplikacija ciroze jetre i direktno ugrožava život bolesnika. Praćenjem kliničkih i laboratorijskih parametara hepatocelularne insuficijencije (*Child-Pugh* skor) moguće je odrediti prognozu bolesnika koji krvare. Model terminalnog stadijuma bolesti jetre (MELD) od nedavno preporučuje se u predikciji mortaliteta kod bolasnika sa cirozom jetre. Cilj rada bio je praćenje prognoze preživljavanja bolesnika sa cirozom jetre MELD i *Child Pugh* skorom i analiza prognostičke vrednosti MELD skora kod bolesnika sa varikoznim krvarenjem. **Metode.** Retrospektivno je analizirano preživljavanje grupe od 100 bolesnika sa cirozom jetre prosečne starosti 57 godina. Za svakog bolesnika izračunavani su *Child-Pugh* i MELD skor. Analizirana je povezanost kliničkih i laboratorijskih parametara hepatocelularne insuficijencije sa petnaestomesečnim preživljavanjem. Korelisane su vrednosti MELD i *Child-Pugh* skora. Statistička obrada podataka vršena je Studentovim *t*-testom. **Rezultati.** U toku petnaestomesečnog praćenja umrlo je 22 bolesnika. Pol i starost bolesnika nisu uticali na stepen preživljavanja. *Child-Pugh* i MELD skor signifikantno su se razlikovali između grupa bolesnika koji su preživeli i onih koji su umrli ($p < 0,0001$). Takođe, nađena je signifikantno značajna razlika prisustva ascitesa i encefalopatije između grupa preživelih i umrlih bolesnika ($p < 0,0001$). Vrednosti INR (International Normalized Ratio), kao i nivoa kreatinina i bilirubina u serumu

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bile su signifikantno veće, a albumina signifikantno manje kod bolesnika koji su umrli ($p < 0,0001$). MELD skor bio je signifikantno veći u grupi bolesnika koji su umrli zbog ezofagusnog varikoznog krvarenja ($p < 0,0001$). **Zaključak.** MELD skor je pouzdan u prognozi preživljavanja bolesnika sa cirozom jetre kao i *Child-Pugh* skor. Porast MELD skora udružen je sa smanjenjem rezidualne funkcije jetre. MELD skorom može da se proceni rizik od intrahospitalnog mortaliteta u grupi bolesnika sa cirozom jetre i ezofagusnim varikoznim krvarenjem.

Ključne reči:
jetra, bolesti; jetra, ciroza; jednjak i želudac, variksi; upitnici; prognoza.

Introduction

Over the years, many clinical and biochemical parameters have been suggested in order to predict more accurately the prognosis of cirrhotic patients and correctly assess their survival rate. They are important because of application of adequate therapy and prioritization of transplantation lists, particularly because of the fact that there is an increasing discrepancy between the number of cirrhotic patients on waiting lists for orthotopic liver transplantation (OLT) and the number of available liver donors [1].

The Child-Pugh score is still considered the cornerstone in prognostic evaluation of cirrhotic patients although it was formulated more than 30 years ago. Nevertheless, it has some drawbacks such as the subjectivity of clinical parameters and a limited discriminatory ability [2, 3]. The Child-Pugh Class A patients usually show a good median survival term without OLT unless other events (such as hepatocellular carcinoma, uncontrolled bleeding due to portal hypertension, etc) occur [1, 4]. The Child-Pugh Class C patients are considered the conventional candidates for the procedure. The Child-Pugh Class B patients can be considered a heterogeneous group, as their clinical condition may remain stable for more than a year or rapidly deteriorate [5].

Recently, the Model for the End-stage Liver Disease (MELD) was introduced as a tool for predicting mortality risk and to assess the severity of the disease in patients with liver cirrhosis, as well as to determine organ allocation priorities [6–12].

Although the MELD score takes into consideration objective parameters (serum creatinine, the International Normalised Ratio – INR, bilirubin levels) and is computed with statistically derived coefficients on a continuous scale with no upper or lower limits, thus avoiding many drawbacks of the Child-Pugh score, it is not being used yet in everyday practice [13, 14].

The aim of the study was to evaluate the survival prognosis of cirrhotic patients and patients with complications by means of the MELD score compared to the Child-Pugh one. We also analysed the prognostic value of the MELD score in patients with both liver cirrhosis and variceal bleeding.

Methods

This retrospective study included cirrhotic patients (76 males, 24 females; median age 57 years, ranging from 32–79) hospitalised due to complications of the disease. Patients with the hepatorenal syndrome, spontaneous bacterial peritonitis and hepatocellular carcinoma were excluded from the study. Liver cirrhosis was diagnosed on the basis of histological, clinical and biochemical results, as well as by echosonographic and endoscopic examination. The etiology of liver disease was hepatitis C virus (HCV) in 4% of the patients, hepatitis B virus (HBV) in 7%, alcohol abuse in 88%, and autoimmunity in 1%. We calculated the Child-Pugh score using an original formula (Table 1) [15].

Table 1

Child-Pugh score parameters

Parameters	1 point	2 points	3 points
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	None	Suppressed with medication	Refractory
Hepatic encephalopathy	None	Grade I–II (or suppressed with medication)	Grade III–IV (or refractory)

INR- International Normalized Ratio

The patients were classified as follows: Class A – 28, class B – 37 and class C – 35 patients. The MELD score was calculated according to the original formula proposed by the Mayo Clinic group: 10 {0.957 Ln [creatinine (mg/dL)] + 0.378 Ln [bilirubin (mg/dL)] + 1.12 Ln INR + 0.643}

Statistical analysis was first performed on the whole group of 100 patients and then on the subgroup of 48 patients with liver cirrhosis and esophageal variceal bleeding, evaluating survival and intrahospital mortality. For statistics we used the Student's *t*-test.

The results were expressed as median (range). Receiver operating characteristic (ROC) curves were used to determine the cut-off values of the Child-Pugh and MELD scores, with the best sensitivity (SS) and specificity (SP) in discriminating between patients who survived and those who

died. The validity of the models was measured by means of concordance (*c*) statistics (equivalent to the area under the ROC curve)[12]. A *c* value of 0.8–0.9 indicated an excellent diagnostic accuracy; a model with a c value > 0.7 was considered useful. For all analyses a *p* value < 0.05 was considered statistically significant. The data were analysed using XL Stat, Microsoft Office Excel, Statistics 6.

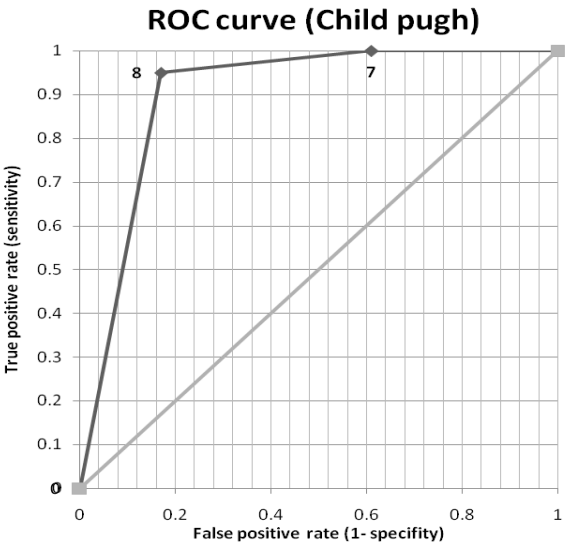

Fig. 1 – ROC curve (the Child-Pugh score)

Results

During a 15-month follow up, 22 patients died, out of whom none from the Child-Pugh Class A (0%), 1 from Class B (3%), and 21 from Class C (58%). The causes of death were all related to liver disease. Seventyeight patients survived more than 15 months: 28 were Child-Pugh Class A (100%), 36 Class B (97%), and 14 Class C (42%).

Clinical and biochemical parameters, the MELD and Child-Pugh scores were presented in Table 2. Age and gender did not affect survival. The Child-Pugh and MELD scores significantly differed in patients who survived from those who died ($p < 0.01$). Ascites and encephalopathy were significantly different in patients who survived as compared to those who died ($p < 0.01$). The values of INR, serum creatinine and bilirubin were significantly higher and albumin significantly lower in patients who died ($p < 0.01$).

Table 2

Clinical and biochemical characteristics, MELD and Child-Pugh scores

Parameters	Surviving patients	Deceased patients	*t*	*p*
Sex (M/F)	59/19	17/5		
Average age (years)	60	55		
Encephalopaty (Yes/No)	12/66	19/3	-8.28	< 0.0001
Ascites (Yes/No)	47/31	18/4	-6.50	< 0.0001
INR	1.445	2.13	-4.52	< 0.0001
Serum albumin (mg/dL)	31.15	26.35	4.56	< 0.0001
Serum bilirubin (mg/dL)	0.401	0.765	-4.93	< 0.0001
Serum creatinine (mg/dL)	0.867	1.225	-5.94	< 0.0001
Variceal bleeding MELD (Yes/No)	39/49	9/13	-5.43	< 0.0001
Child-Pugh score	7	12	-10.90	< 0.0001
MELD score	5.457	18.42	-7.33	< 0.0001

INR - International Normalized Ratio; Child-Pugh score – see Table 1;
MELD - Model for the End-stage Liver Disease = 10 {0.957 Ln [creatinine (mg/dL)] + 0.378 Ln [bilirubin (mg/dL)] + 1.12 Ln INR + 0.643}

A calculated sensitivity and specificity of the MELD and Child-Pugh score showed that both methods are highly sensitive, but the MELD score had a lower specificity for predicting survival prognosis (Figures 1 and 2). The cut-off values with the best SS and SP, the Child-Pugh and MELD scores were calculated using ROC curves. We also calculated the *c* value using ROC curve. The *c* values were 0.89 for Child-Pugh score and 0.84 for MELD score (Table 3.)

In the group of 48 patients with esophageal variceal bleeding, 9 (19%) died and 39 (81%) survived. The MELD score in patients who died was significantly higher than the MELD score in patients who survived. The *c* value was 0.71. Most of the patients died within five days after the admission.

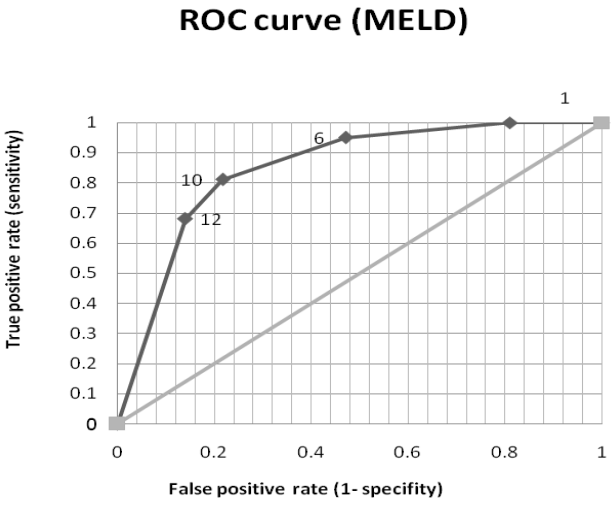

Fig 2 – ROC curve (the MELD score)

Table 3

Sensitivity, specificity, c-value of MELD and Child-Pugh scores

Score	Cut-off	Sensitivity (%)	Specificity (%)	*c* – value
Child-Pugh	8	95.45	82.05	0.89
MELD	6	95.45	53.84	0.84

MELD- Model for the End-stage Liver Disease

Discussion

Prognostic evaluation of patients with liver cirrhosis is an important topic often challenging clinicians. Correct timing of liver transplantation can reduce the mortality of patients on waiting lists and improve post-transplant survival [16-19]. Predicting prognosis is important for further plan of treatment, especially in patients with esophageal variceal bleeding. The Child-Pugh score is an important component of the prognostic evaluation of cirrhotic patients, although this traditional score has several shortcomings such as subjectivity of some parameters and a limited discriminatory ability. In order to overcome the limits of the Child-Pugh score, previous studies have evaluated a "combined score" with quantitative liver function tests, or have applied the scores that were originally formulated to evaluate multiorgan insufficiency in critically ill patients to cirrhotic patients [20–22].

Recently, a study group at the Mayo Clinic introduced a new scoring system, called MELD, to evaluate the prognosis in patients with liver cirrhosis. Two independent studies performed in North American cirrhotic patients showed that the MELD score performed at least as well as the Child-Pugh score in predicting patient outcome following acute variceal bleeding and mortality in patients referred for liver transplantation [23, 24]. In this study our objective was to evaluate survival prognosis in patients with liver cirrhosis by comparison of the two groups of patients: patients with liver cirrhosis who died, and those who survived for 15 months. We compared the MELD and Child-Pugh scores and each parameter separately between these two groups in order to assess their significance. Finally, we compared the MELD scores in patients who survived esophageal bleeding with those who died. By comparison of the MELD and Child-Pugh scores of the surviving patients to those who died we found a statistically significant difference. A multivariate analysis showed that signs of liver decompensation, such as the presence of ascites, higher values of INR, serum bilirubin and creatinine levels and encephalopathy, were independently associated with a 15-month mortality; our analyses showed a statistically significant difference between the two groups. Age and gender did not affect survival. We calculated sensitivity and specificity of the MELD and Child-Pugh scores and showed that both methods are highly sensitive, but that the MELD has lower specificity in predicting the survival prognosis. The *c* values were 0.89 for the Child-Pugh score and 0.84 for the MELD score implying an excellent diagnostic assessment. Finally, we analysed the group of patients with variceal bleeding and computed the MELD score for each patient. The MELD score was statistically significantly higher in patients who died due to variceal bleeding. Using the ROC curve we found the cut-off value of the MELD score to be 16, and the *c* value 0.71, which showed good prognostic accuracy.

Conclusion

The MELD and Child-Pugh scores are highly sensitive methods in predicting survival prognosis in patients with both liver cirrhosis and variceal bleeding.

Increase in the MELD score is associated with decrease in the residual liver function. In cirrhotic patients with esophageal variceal bleeding the MELD score identifies a group of patients with a higher risk of in-hospital mortality.

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The paper received on January 20, 2009